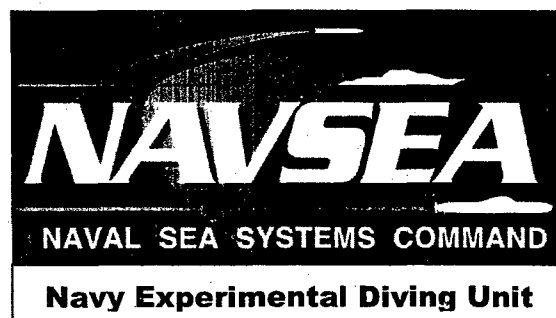


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REPEATED SIX-HOUR DIVES WITH 1.35 ATM OXYGEN PARTIAL PRESSURE



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INTRODUCTION

The *U.S. Navy Diving Manual* currently limits the use of oxygen in diving to a maximum of four hours in a 24-hour period.¹ Technical limitations no longer restrict dive lengths to four hours, and for some operations, longer dives may be useful. This report details some effects of multiple six-hour underwater exposures to oxygen partial pressure (P_{O_2}) of 1.35 atmospheres (atm), as specified in the task *Pulmonary Oxygen Toxicity after Repeated Diving with Elevated Oxygen Partial Pressures*.²

We have studied pulmonary effects of dives with eighteen hours between them (dives synchronized to time of day) on each of two days or on each of five days, and of dives every other day for six days (dives with 42-hour recovery times). We have also studied two daily exposures of six hours, but with the six hours split into two 3-hour dives with three different surface intervals. These dive series are reported here. We have reported previously on single six-hour dives where divers breathed oxygen at a partial pressure of 1.35 atm,³ and single six-hour dives in water or in the dry chamber where divers breathed oxygen at a partial pressure of 1.6 atm.⁴

In all studies we measured pulmonary function and assessed symptoms immediately after diving and for several days after the exposures. The pulmonary function variables were forced vital capacity (FVC), forced expired volume in one second (FEV_1), peak expired flow (maximum forced expired flow, FEF_{max}), mid expiratory flow (FEF_{25-75}), and diffusing capacity of the lung for carbon monoxide (D_LCO). The lower limits of normal for pulmonary function variables were defined as decreases from baseline of 2.4 times the coefficient of variation found for the Navy Experimental Diving Unit (NEDU) population — namely, 7.7% for FVC, 8.4% for FEV_1 , 16.8% for FEF_{max} , 17.0% for FEF_{25-75} , and 14.2% for D_LCO .³ We defined decreases of these magnitudes, the lower 95% confidence bands for each variable, as the lower limits of normal.

We did not measure visual refraction daily during the pairs of daily dives or five daily dives, but we checked distance vision with a wall chart after the entire dive series. We measured refraction daily during the dive series with 42 hours between dives and during the split (short surface interval) exposures.

METHODS

GENERAL

Thirteen divers dove in the series of dives on two consecutive days; 17 began the series of five consecutive daily dives, and 16 completed it. Sixteen began the series of six dives every other day, and 13 completed it; and 48 divers completed two days of split exposures: 12 with a two-hour surface interval (SI) each day and 16 hours overnight; 24 with a four-hour SI each day and 14 hours overnight; and 12 with a six-hour SI each day and 12 hours overnight. Many divers participated in more than one series, and several dove more than once in a single series. The series of six dives every other day was

done in two sections about 18 months apart, and one subject dove it both times. The protocols were approved NEDU Institutional Review Board, and all subjects gave written informed consent.

Table 1. Subject Characteristics, by study

a) Two dives, 18-hr interval		Median	Minimum	Maximum
	Age (yrs)	39	28	48
	Height (in)	69	66	74
	Weight (lbs)	188	158	220
	Smoking (#)	<i>never, 7; former, 6; current, 0</i>		
	Respiratory allergies (#)	3	(Subjects E, K, I)	
	Current	1	(Subject I)	
	Anti-inflammatory medication (#)	3	(Subjects B, C, J)	
	Decongestant	1	(Subject I)	
b) Five dives, 18-hr interval		Median	Minimum	Maximum
	Age (yrs)	35	27	45
	Height (in)	70	68	76
	Weight (lbs)	193	160	248
	Smoking (#)	<i>never, 12; former, 3; current, 1 (Subject V)</i>		
	Respiratory allergies (#)	4	(Subjects Q, S, U, X)	
	Current	0		
	Anti-inflammatory medication (#)	4	(Subjects B, T, U, W)	
c) Six dives, 42-hr interval		Median	Minimum	Maximum
	Age (yrs)	36	30	43
	Height (in)	69	68	74
	Weight (lbs)	190	158	230
	Smoking (#)	<i>never, 7; former, 7; current, 0</i>		
	Respiratory allergies (#)	2	(Subjects Q, X)	
	Current	0		
	Anti-inflammatory medication (#)	2	(Subjects B, AE)	

d) 3-hr dives, 2-hr SI, 16 hrs overnight		Median	Minimum	Maximum
	Age (yrs)	42	27	46
	Height (in)	69	67	74
	Weight (lbs)	195	152	215
Smoking (#)	<i>never, 5; former, 7; current, 0</i>			
Respiratory allergies (#)	3 (Subjects Q, AJ, AL)			
Current	1 (Subject AJ)			
Anti-inflammatory medication (#)	3 (Subjects AJ, AM, AN)			

e) 3-hr dives, 4-hr SI, 14 hrs overnight		Median	Minimum	Maximum
	Age (yrs)	35	24	46
	Height (in)	69	67	75
	Weight (lbs)	195	152	235
Smoking (#)	<i>never, 13; former, 11; current, 0</i>			
Respiratory allergies (#)	9 (Subjects U, X, AL, AP, AV-AZ)			
Current	0			
Anti-inflammatory medication (#)	3 (Subjects U, AM, AR)			
Antihistamines (#)	1 (Subject AY)			

f) 3-hr dives, 6-hr SI, 12 hrs overnight		Median	Minimum	Maximum
	Age (yrs)	38	33	42
	Height (in)	71	68	73
	Weight (lbs)	193	152	262
Smoking (#)	<i>never, 5; former, 6; current, 1 (Subject BD)</i>			
Respiratory allergies (#)	6 (Subjects U, X, AL, AP, AY, BC)			
Current	0			
Anti-inflammatory medication (#)	1 (Subject U)			
Antihistamines (#)	1 (Subject AY)			

The dives, which were conducted in fresh water in the 15-foot deep NEDU test pool, were controlled and supervised by qualified NEDU personnel. Subjects rested underwater while breathing surface-supplied, humidified oxygen open circuit from MK 20 underwater breathing apparatus (UBA) full face masks. During the dives, because the demand regulators were at a depth between 11 and 12 feet of fresh water, they provided oxygen partial pressures between 1.32 and 1.35 atm. (The absolute pressure at the bottom of the test pool was 1.44 atm.)

Before the study, subjects had not been diving for at least one week. Except for their experimental dives, they refrained from diving throughout the study. Each subject's smoking behavior and history of respiratory allergies were noted. General health and use of medications also were recorded.

The subjects performed pulmonary function tests several days before the test dives, immediately before diving, within 60 minutes of leaving the water, between the dives that were conducted every other day, and on working days until the third or fourth day after the test dives. If pulmonary function variables on the last of these days were below the 95% confidence bands of baseline, they were measured again on the next day and then, if necessary, approximately one week later to confirm that they had returned within normal limits. Each pulmonary function measurement session involved three repetitions of each scheduled test that each met American Thoracic Society standards.⁵

In the mornings before dives, between the three-hour dives, and after the first days of the split exposure studies, we measured flow-volume loops but not diffusing capacity. At all other sessions, we measured both flow-volume loops and diffusing capacity. Blood samples were drawn in conjunction with most diffusing capacity measurements, but on the second and later days after diving, we used hemoglobin and carboxyhemoglobin values from the first day without a dive. Divers were questioned about specific symptoms (Table 2) while they were underwater and at each pulmonary function measurement session.

Table 2. Symptoms list

During the dives:	After the dives:
Vision changes	Inspiratory burning
Ringling or roaring in ears	Cough
Nausea	Chest pain or tightness
Tingling or twitching	Shortness of breath
Light-headedness or dizziness	Lowered exercise tolerance
Chest tightness	Unreasonable fatigue
Shortness of breath	
Rapid shallow breathing	
Burning on inspiration	
Cough	

During the week before diving and during the week following their last dives, divers who enrolled in the series of six dives every other day were referred to the Tyndall Air Force Base optometry clinic for complete eye examinations, including internal and external ocular examination, cycloplegic refraction, a fundoscopic photograph, and measurements of corneal curvature and intraocular pressure. With those divers and with those in the split exposure dives (short surface intervals) we also used an

automatic refractometer to measure visual refraction when we measured pulmonary function.

EXPERIMENTAL DESIGN AND ANALYSIS

Incidences of symptoms and of changes in pulmonary function were compared pairwise across dives with Fisher's Exact Test. For example, the incidence of changes subsequent to a first six-hour dive was compared to that following the first day with two three-hour dives. Comparison was also made to the incidences after four-hour dives at the same PO_2 .⁶ Incidences were considered to differ significantly if $p < 0.05$, and marginally if $p < 0.10$.

EQUIPMENT AND INSTRUMENTATION

The Collins CPX and Collins GS Modular Pulmonary Function Testing System instruments (Ferraris Respiratory; Louisville, CO) were used to measure pulmonary function. To measure D_LCO the equipment uses a test gas containing 0.3% carbon monoxide (CO) and 0.3% methane. Volume calibration with a three-liter syringe and two-point gas analyzer calibration (test gas and room air) were performed daily before testing began. A CO oximeter (Instrumentation Laboratory; Lexington, MA) determined carboxyhemoglobin and hemoglobin concentrations from a venous blood sample. An automatic refractometer (Model 530, Allergan Humphrey; San Leandro, CA) was used to measure visual refraction.

Divers breathed surface-supplied oxygen from MK 20 open circuit UBAs. The oxygen was humidified by being passed through bubblers built for the purpose. We confirmed that the passing gas stream had absorbed water by measuring the water volume before and after some of the dives. Communication units were included in the UBA face masks.

PROCEDURES

Before each dive the diver subjects reported to the laboratory, where flow-volume loops were measured; any diver for whom any flow-volume loop variable had decreased by twice the 95% confidence band was to be prohibited from diving. For subjects who dove for six days or with short surface intervals, visual refraction was checked before dives. Any diver for whom refraction had changed by -0.5 diopters (D) or more from baseline also was to be withdrawn from the dive series.

Under the dive supervisor's direction, the diver subjects then entered the water at about 10-minute intervals. During the dives, subjects relaxed in lounge chairs or directly on the bottom of the test pool, where they watched movies. During the six-hour dives they surfaced to eat or drink and to breathe room air for no more than five minutes per hour, but for the three-hour dives they remained on the bottom unless they had to surface. Water temperature was 90 ± 5 °F (32 ± 3 °C). Divers were dressed for comfort — most

in swim trunks and T-shirts, but a few in wet suits. They were questioned about specific symptoms (Table 2) once per hour while they were underwater.

At the end of the six hours, or three hours for the split exposures, divers were instructed to surface and leave the water. During their first ten minutes on the surface, they were escorted as a precaution in case of arterial gas embolism. During or after the ten-minute period, a blood sample was drawn to measure hemoglobin and carboxyhemoglobin, visual refraction was tested, and pulmonary function was measured. Additionally, the divers completed the postdive questionnaire and instilled a solution of 2% acetic acid and aqueous aluminum acetate into their ear canals to reduce the chance of infection.

To record flow-volume loops, a subject wearing nose clips breathed on a mouthpiece into and out of the spirometer. The subject first breathed normally, then inhaled rapidly and as fully as possible before exhaling with maximum force and inhaling fully again. Measurements of FVC, FEV₁, FEF_{max}, and FEF₂₅₋₇₅ were read from the flow-volume loops.

The single-breath technique was used to measure D_LCO: the subject exhaled as far as possible, inhaled as much of the test gas from the spirometer as possible, held his breath for 10 seconds, then exhaled briskly past the analyzer sample port. The variables used to obtain D_LCO were calculated from the gas concentrations before and after the breath hold. Adjustments were made for carboxyhemoglobin and hemoglobin concentrations.⁷ Volumes expired before the gas concentrations were measured and volumes of gas over which the concentrations were averaged were adjusted to ensure that the analyzer signal was stable when measurements were recorded.⁸

Refraction was measured one eye at a time while subjects looked into the automatic refractometer. Both spherical and cylindrical refractions were read in increments of 0.25 D, and axes were read in increments of one degree. We took triplicate measurements at baseline and after the dives and averaged them, but we used only single predive measurements to assess whether a subject could dive. If a reading was 0.5 D or more below the baseline average, two other readings were taken and their average was used to confirm whether the abort condition had been met.

RESULTS

HUMIDIFIERS

When we measured the volumes of water evaporated from the humidifiers, we found an average of 3.2 mL per diver per hour during the dives (range 2.50 to 3.65 mL). Because we did not measure the temperature of the gas stream leaving the bubblers or the volume of gas passing through them, we can only estimate humidity. When the gas temperature is 20 °C, the saturated vapor pressure of water is 17.5 Torr and the saturated vapor density is $17.3 \text{ g} \cdot \text{m}^{-3}$. If each diver is assumed to have had a minute ventilation of 6 L/min, then each breathed 0.36 m^3 every hour, gas which could have contained 6 g water if it had been saturated at 20 °C. With these figures, the relative humidity leaving the bubblers ranged from 53% to 61%.

PULMONARY EFFECTS

Several subjects participated in more than one dive series, and not always with similar results. In the example of Figure 1, Subject X showed decreased FEV_1 and FEF_{25-75} after the fifth but not after the sixth dive during the series of six dives every other day, and no change during the series of five daily dives, except for a drop in FVC on the third day after the end of the dive series. The subject reported scattered symptoms during both dive series (Tables 5 and 6).

Pulmonary results from the dives are shown in Tables 4–7. Subject identifiers are arbitrary but are consistent throughout this report. Pulmonary function variables found to be low after a dive or before the next dive are listed under the dive most closely preceding the finding. If a value was low both immediately after a dive and the following morning before the next dive, the greater difference from baseline is listed. Symptoms also are listed under the dive that most closely preceded their report and under the most severe class that applies.

Most subjects were very consistent in performance of the pulmonary function tests, producing three almost superimposable flow-volume loops each time. Subject AO, however, had difficulty in performing the maneuvers. Both his technique and his effort seemed to vary. During the series of two 3-hour dives with 4-hour SI, the only dive series in which he participated, his FEV_1 on the morning of the second day was sufficiently low in the best three of six attempts that he was to have been excluded from diving (Table 7b). He asked to try again, showed normal values for all parameters, and was permitted to continue with the series. Both sets of values have been reported in Table 7, but the second set was considered correct.

INCIDENCES OF RESPIRATORY SYMPTOMS AND SIGNS

Overall in this study, single six-hour dives at $PO_2 = 1.35$ atm were completed 52 times, and pairs of dives with 18 hours between them were completed 29 times. The overall incidences of symptoms and signs immediately after the first 6-hour dive of a series were 33% (binomial 95% confidence interval [CI]: 20% to 46%), 4% (95% CI: 0.5% to 13%), and 6% (95% CI: 1% to 16%) for mild symptoms, moderate symptoms, and changes in flow-volume loops, respectively. Immediately after two dives the incidences were 34% (95% CI: 18% to 54%), 10% (95% CI: 2% to 27%), and 3% (95% CI: 0.1% to 18%). The incidences of symptoms were greater than those after one or two 4-hour dives:⁹ 17% and 14% (Fisher's Exact $p = 0.04$). Incidences of flow-volume loop changes were not different from those after one or two four-hour dives: 5% and 18%, apparently but not significantly higher after two four-hour dives than after two six-hour dives. There were no changes in diffusing capacity after one or two six-hour dives.

When diving continued for five days, the incidences of mild symptoms in the much smaller sample of sixteen divers remained similar to those after one or two dives, at 44%, 50%, and 31% after the third, fourth, and fifth dives, respectively. Symptoms worse than mild were reported by only one subject (6% incidence) and only after his fifth dive. Flow-volume loop changes were seen in 25%, 6%, and 6% of the subjects after Dives 3, 4, and 5, respectively, possibly an increase in incidence after three, as compared to two, dives (Fisher's Exact Test $p = 0.047$). Changes in diffusing capacity were measured in 6% and 13% of the subjects after Dives 4 and 5, respectively.

When diving was conducted every other day for six days, symptoms were reported by 14%, 29%, 50%, 28%, and 28% of subjects after Dives 2 through 6, respectively. Moderate symptoms were reported by two subjects (14%) after Dive 4 and by one subject (7%) after Dive 5. Flow-volume changes were measured in 36%, 21%, 36%, 15%, and 15% of the subjects after Dives 2 through 6, respectively, and changes in diffusing capacity were measured in one subject after each of Dives 2 and 3. Only the second dive with 42 hours between dives differs in incidences from the second with 18 hours between dives: the incidence of symptoms is marginally greater (Fisher's Exact $p = 0.05$ one-sided, 0.09 two-sided), and the incidence of pulmonary function change is significantly greater (Fisher's Exact $p = 0.01$). The incidence of symptoms after two six-hour dives with 42 hours between dives is no different from the incidence after two four-hour dives with 20 hours between them.

The incidences of symptoms when the exposures were split into two dives with short SIs between them on the first day were 42%, 17%, and 25% for the two-, four-, and six-hour SIs, and on the second day they were 50%, 13%, and 42%, again for increasing SI. Only after the four-hour SI did incidences differ from those for six-hour dives; fewer subjects reported symptoms after those dives than after the six-hour dives, marginally fewer after one day (Fisher's Exact $p = 0.03$ one-sided, 0.06 two-sided), and significantly fewer after two days of diving (Fisher's Exact $p = 0.011$ one-sided, 0.016 two-sided). The incidences of symptoms with the four-hour SI did not differ on either

dive day from those after four-hour dives with 20 hours overnight. The incidences of moderate symptoms on the first and second days (with one subject in each case) were 8% and 4% for the two- and four-hour SIs.

Flow-volume loops after the short SI dive days were changed on the first day in 2%, 25%, and 33% of the subjects with 2-, 4-, and 6-hour SIs, respectively. On the second day flow-volume results were changed in no one after the 2-hour SI and in 17% of the subjects with either the 4- or 6-hour SIs. The 33% incidence was statistically greater than the 3% incidence of flow-volume changes seen after a single six-hour dive (Fisher's Exact $p = 0.02$). For diffusing capacity, which was measured after the split exposure dives only on the second day of diving and later, changes were seen in one subject (8%) after the 2-hour SI dives and in one subject after the 6-hour SI dives (8%).

The incidences of symptoms and signs on the first or later postdive day at the end of each dive series are given in Table 3.

Table 3. Incidences of symptoms and signs at least one day postdive
Values in parentheses are binomial 95% confidence intervals.

* indicates the only two values that are significantly different.

	Dives on two consecutive days				Dives on 5 consecutive days	Dives on 6 alternate days
	6-hour dives	Two 3-hour dives				
		2-hr SI	4-hr SI	6-hr SI	6-hour dives	6-hour dives
Symptoms	15%	16%	0%	8% (1 diver)	25%* (7% – 52%)	0%*
Flow-volume changes	23% (5% – 54%)	8%	8%	17%	25%	15%
D _L CO changes	23%	0%	8%	17%	6%	8%

Table 4. Respiratory symptoms, decreases from baseline in pulmonary function:
Two 6-hour dives, 18-hour interval

n = 13	Dive 1	Dive 2	Day + 1	Later
Subject A	Hr 2: i i, c	Hr 1: i, c	D _L CO -15.2% i, c	D _L CO -15.7% i
Subject B	Hr 1: c c	Hr 1: c c	c	c
Subject C		c		FVC -9.5% FEV ₁ -10.0% c
Subject D	i, c	i	FEV ₁ -9.9%	
Subject E	Hr 5: c ; Hr: 1 t	c, t	FEV ₁ -9.1% c, t, d	
Subject F				D _L CO -14.3%
Subject G	FVC -8.6%			FEV ₁ -8.6%
Subject H	Hr 1: i i, c	Hr 1: i, c i, c		D _L CO -14.3%
Subject I				FEF ₂₅₋₇₅ -17.4%
Subjects J-M	none			

Symptoms: t = chest tightness, i = inspiratory burning, d = dyspnea, c = cough

Symptoms listed in roman face were mild, and those in **bold** were moderate. "Later" records events more than one day after the second dive. Symptoms reported during a dive are prefaced by the hour when they began, and those after a dive have no prefix.

Table 5. Respiratory symptoms, decreases from baseline in pulmonary function:
Five 6-hour dives, 18-hour interval

n = 16	Dive 1	Dive 2	Dive 3	Dive 4	Dive 5	Later
Subject B	t	i, t	Hr 6: c FEF ₂₅₋₇₅ -22.4% t, d	Hr 2: i i, t	Hr 1: t, d t	FEF ₂₅₋₇₅ -19.9% i, c, t
Subject N			T			
Subject O				D _L CO -15.2%		D _L CO -14.9%
Subject P			FVC -8.1% FEV ₁ -11.0% FEF ₂₅₋₇₅ -19.8%	FVC -10.1%	FVC -9.3%	FVC -12.3% FEV ₁ -14.1% FEF ₂₅₋₇₅ -21.1%
Subject Q	i, t		FEV ₁ -9.6% FEF ₂₅₋₇₅ -24.3%	t		FEV ₁ -17.7% FEF ₂₅₋₇₅ -36.3% t, d
Subject R	c	c	Hr 6: i i, c, t			
Subject S	t	Hr 3: t, i, d, c i, t, d, c	Hr 4: t Hr 6: d c, t	c	Hr 6: d, c c, t, d	
Subject T			FEF _{max} -21.5%	t	t	
Subject U		Hr 5: i		t	t	
Subject V		Hr 4: i, t FEF ₂₅₋₇₅ -18.2% i, c, t			Hr 3: t D _L CO -19.9% t	
Subject W	i	i	Hr 6: i t	t	i, t	
Subject X			t	t, c		FVC -8.2% t, c
Subject Y	t	t, i, c, d	c, t			FVC -11.0%
Subject Z		i		t	D _L CO -15.1% i, t	i, t
Subjects AA, AB	none					

Symptoms: t = chest tightness, i = inspiratory burning, d = dyspnea, c = cough
Symptoms in roman face were mild, those in **bold** were moderate, and those in *italic bold* were moderately severe. "Later" was at least three days after Dive 5.

Table 6. Respiratory symptoms, decreases from baseline in pulmonary function:
Six 6-hour dives, 42-hour interval

n = 14	Dive 1	Dive 2	Dive 3	Dive 4	Dive 5	Dive 6	Later
Subject A	Hr 2: i		Hr 2: i	Hr 3: i, c	Hr 1: i	Hr 3: i i, c	
Subject B		FEV ₁ -8.6% D _L CO -14.3%	i	FEV ₁ -8.6%			
	c						
Subject H*			Hr 4: i i	i	Hr 5: i i, t	Hr 4: i i, d	
Subject L*		FEV ₁ -9.4% FEF ₂₅₋₇₅ -18.0%					
Subject M			FVC -10.3% FEV ₁ -13.9% FEF ₂₅₋₇₅ -27.2%	Hr 1: t Hr 5: c FVC -10.0% FEV ₁ -13.9% FEF ₂₅₋₇₅ -28.0% i, c, t		FEF ₂₅₋₇₅ -19.4%	FEF ₂₅₋₇₅ -18.0%
	i, c						
Subject Q		FEV ₁ -9.2% FEF ₂₅₋₇₅ -18.4%		c, t, d	t, d		
Subject X*					FEV ₁ -10.8% FEF ₂₅₋₇₅ -20.0%		
Subject Z*			FVC -7.8%	Hr 5: i FVC -8.8% i	Could not continue to dive because of severe ear pain.		
		i, t					
Subject AC	i, c	i, c, t	i, c, t	i, c	i, c, t	i	D _L CO -16.8%
Subject AD		FEF _{max} -17.9%	DLCO -14.3%	FEF _{max} -17.9% i, c	FEF _{max} -20.1%	FEF _{max} -20.6% i, c	FEF _{max} -21.0%
Subject AE*	FEF ₂₅₋₇₅ -19.5%	FEF ₂₅₋₇₅ -21.0%	FEF ₂₅₋₇₅ -20.3%	FEF ₂₅₋₇₅ -19.7%			
Subjects AC2*, AF*, AG*				none			
AC2 is second dive set for subject AC.							

Symptoms: t = chest tightness, i = inspiratory burning, d = dyspnea, c = cough
Symptoms in roman face were mild, and those in **bold** were moderate. "Later" includes one day after diving. * August 2005 dives (second set)

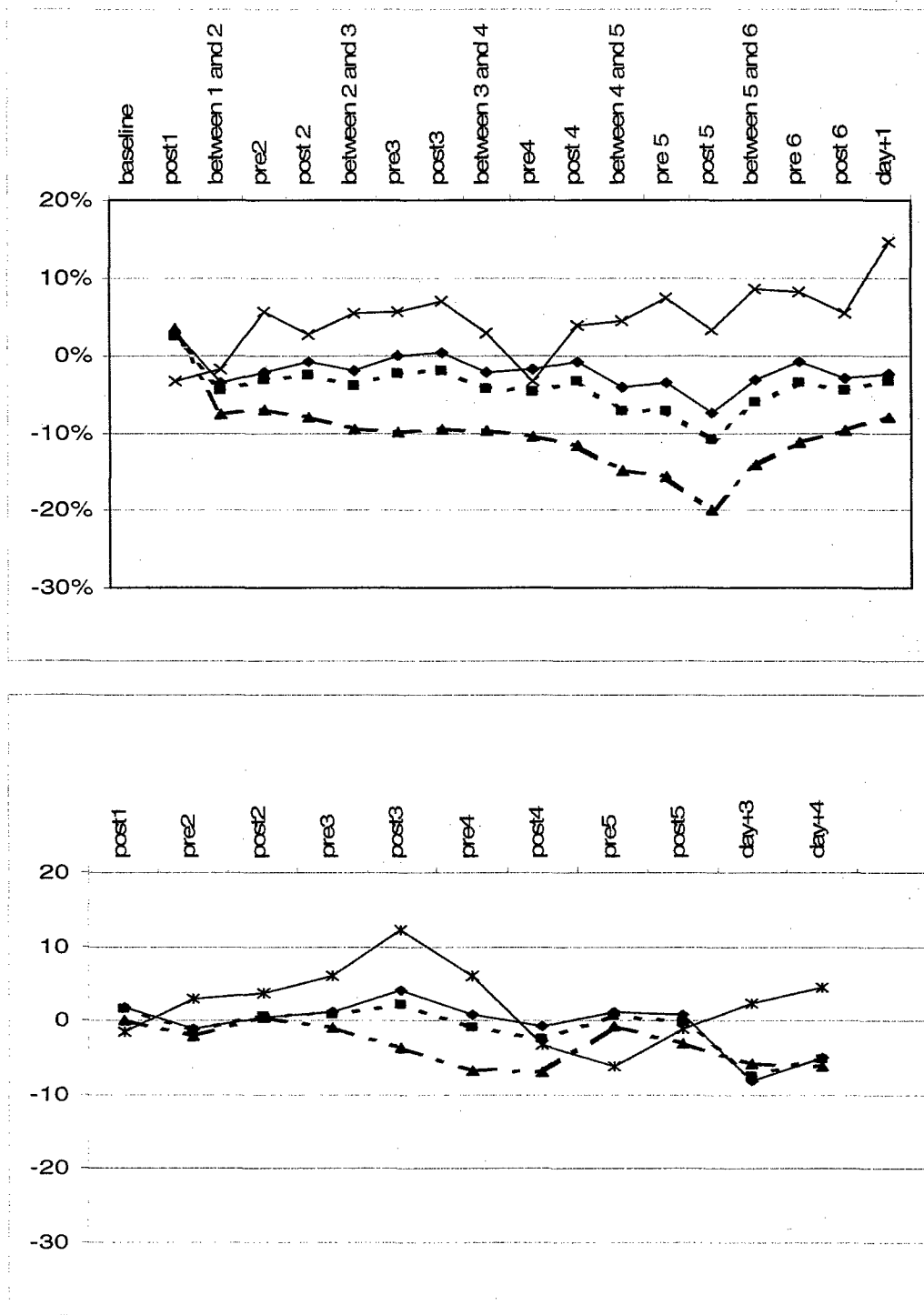


Figure 1. Time course of flow-volume parameters, subject X
 ◆ and thin solid line, FVC; ■ and thick dotted line, FEV₁; x and thin solid line, FEF_{max}; and ▲ and thick broken line, FEF₂₅₋₇₅. Top panel: every other day, bottom panel, every day.

Table 7. Respiratory symptoms, decreases from baseline in pulmonary function:
Two days with a three-hour dive, a short surface interval, then a second three-hour dive
a) SI = 2 hours, then 16 hours

n = 12	Dive 1, day 1	Dive 2, day 1	Dive 1, day 2	Dive 2, day 2	Later
Subject H		Hr 1: i i		i	
Subject Q		i, c , d, t	i, c, t	Hr 1: c i, c, t	i, t, d , c
Subject AA					FVC -12.7% FEV ₁ -10.7%
Subject AH			c		c
Subject AI		FVC -11.4% FEV ₁ -12.9% FEF ₂₅₋₇₅ -20.0% t	Hr 3: t	Hr 1: t t	
Subject AJ				D _L CO -17.2% c, t	
Subject AK		i, t	Hr 3: i	Hr 1: i, t i, t	
Subject AL		FEF _{max} -17.8%			
Subject AM	Hr 2: t i, t	Hr 1: t i, t			
Subjects M, AG, AN		none			

Symptoms: t = chest tightness, i = inspiratory burning, d = dyspnea, c = cough
Symptoms in roman face were mild, those in **bold** were moderate, and those in ***italic bold*** were moderately severe. "Later" includes one day after diving.

b) SI = 4 hours, then 14 hours

n = 24	Dive 1, day 1	Dive 2, day 1	Dive 1, day 2	Dive 2, day 2	Later
Subject H			FEV ₁ -11.1% FEF ₂₅₋₇₅ -23.1%		
Subject U	d	d, c		d, c	
Subject AH					D _L CO -15.2%
Subject AK				<i>i</i>	
Subject AO	FEF ₂₅₋₇₅ -19.2%	FEV ₁ ** #1 -19.4% #2 +4% FEF ₂₅₋₇₅ ** #1 -47.3% #2 +2%			
Subject AP				<i>i</i>	
Subject AQ					FEV ₁ -10.5% FEF ₂₅₋₇₅ -18.4%
Subject AR			FVC -8.4% FEV ₁ -12.4% FEF ₂₅₋₇₅ -28.0%	FEV ₁ -9.2% FEF ₂₅₋₇₅ -23.7% D _L CO -17.3%	D _L CO -19.0%
Subject AS	FVC -14.1% FEV ₁ -17.3% FEF ₂₅₋₇₅ -28.2% c			FVC -8.9% FEV ₁ -10.8% FEF ₂₅₋₇₅ -18.2%	
Subject AT		FEF _{max} -16.9% d, t		FEF _{max} -16.8%	FEF _{max} -16.8%
Subjects L, X, Z, AA, AG, AL, AM, AU-AZ, BA			none		

Symptoms: t = chest tightness, i = inspiratory burning, d = dyspnea, c = cough

Symptoms in roman face were mild, those in **bold** were moderate, and that in ***italic bold underlined*** was severe. "Later" includes one day after diving.

** Results of 3 consistent tests both times, with 45 minutes between them (see page 7).

c) SI = 6 hours, then 12 hours

n = 12	Dive 1, day 1	Dive 2, day 1	Dive 1, day 2	Dive 2, day 2	Later
Subject U		c, d		c, d	
Subject X		FEF _{max} -22.4%		c	
Subject Z				D _L CO -16.1% i	
Subject AP					D _L CO -18.8%
Subject AY		FEF ₂₅₋₇₅ -21.7%	FEF ₂₅₋₇₅ -18.0%	FEF ₂₅₋₇₅ -18.0%	FEF ₂₅₋₇₅ -23.6%
Subject BA			FEF ₂₅₋₇₅ -17.3%		D _L CO -15.3%
Subject BB	FEF ₂₅₋₇₅ -18.1%	t		t	
Subject BC	FVC -11.0% FEV ₁ -10.9%	FEF ₂₅₋₇₅ -18.0% c	c	c	FEF ₂₅₋₇₅ -22.0% c
Subjects AF, AL, AU, BD			None		

Symptoms: t = chest tightness, i = inspiratory burning, d = dyspnea, c = cough
All symptoms were mild. "Later" includes one day after diving.

Table 8. Respiratory symptoms, decreases from baseline in pulmonary function:
Single dives, previously reported² and one addition, for comparison

n = 9	Dive 1	Day + 1	Later
Subject D	c		
Subject AA		FVC -7.8% FEV ₁ -8.5%	FVC -8.6% FEV ₁ -10.5%
Subject 3	FEF _{max} -30.5%	FEF _{max} -33.2%	
Subject 4	i, c		
Subject 5	Hr 3: i		
4 subjects, including AW		None	

Numerical subject index is independent of the other tables and represents only subjects who did not dive in the other protocols reported here.

FATIGUE

After diving for six hours on two successive days, four of the thirteen subjects (31%; 95% CI: 9% to 61%) reported unreasonable fatigue. For Subject H, the fatigue was mild and only on the first day after diving; for Subject I it was moderate on the first day after diving and accompanied by severe sleep disturbances; for Subject A it lasted three days and was moderate for two days and mild for one; and for subject E it was severe for three days. After the two-hour surface interval dives, no subject reported fatigue. After the four-hour surface interval dives, Subjects AK, AP, AR, and AU (17%; 95% CI: 5% to 37%) among the 24 divers reported mild fatigue. After the six-hour surface interval dives, three of twelve subjects (25%; 95% CI: 5% to 57%) were unreasonably tired, with Subjects U and Z reporting mild fatigue and Subject AU reporting moderately severe fatigue. None of these proportions differs statistically from any of the others.

After diving for five successive days, nine of sixteen divers (56%; 95% CI: 30% to 80%) reported unusual fatigue or exercise intolerance. Subject N reported mild fatigue on the three days following the dives; Subject O reported moderately severe exercise intolerance on the fifth day of diving and mild exercise intolerance on the third day following the dives; Subject Q had moderate fatigue after the second dive and moderately severe exercise intolerance on the third and fourth days afterwards; Subject R had mild exercise intolerance on the third day after the dives; Subject S had mild fatigue after the second dive and mild exercise intolerance on the third and fourth days after the dive series was over; Subjects T, U, and V reported moderate exercise intolerance on the third day after the dives; and Subject AA had moderately severe fatigue after his second dive.

Five of fourteen subjects (36%; 95% CI: 16% to 65%) reported unusual fatigue or exercise intolerance after the series of six dives every other day. Subject B reported mild fatigue on the days following Dives 2 and 4; Subject H mentioned mild fatigue the day after Dive 2 and moderately severe fatigue the day after Dive 5; Subject Q complained of mild fatigue the day after Dive 1, mild fatigue and moderate exercise intolerance the day after Dive 5, mild fatigue and exercise intolerance after Dive 6, and mild exercise intolerance the day after Dive 6; Subject AC experienced moderate fatigue the day after Dive 1, mild fatigue the days after Dives 2, 3, and 4, and moderate fatigue the day after Dive 5, but only the first time he dove the profile; and Subject AF reported mild exercise intolerance between Dives 1 and 2 and Dives 2 and 3.

EFFECTS ON VISION

We observed no significant visual changes after two successive days with six-hour exposures to $PO_2 = 1.35$ atm for either two days with one dive each or two days with two dives each. For the six-hour dives we simply screened acuity with a wall chart, while for the short surface interval dives we measured refraction.

Significant vision changes occurred after the series of five daily dives. For three subjects, the changes lasted more than four days: Subject X showed a change from

20/25 and 20/30 at baseline to 20/30 and 20/40 on the day of his fifth dive, a change that resolved very slowly; Subject Y showed a change in only one eye from 20/16 at baseline to 20/20 after five days of diving, a change progressing to 20/25 three days after the last dive and returning to 20/16 by 10 days after the last dive; and Subject AA showed a change in acuity for both eyes from 20/16 at baseline to 20/40 on the fifth day after his last dive and lasting for approximately twelve days.

Other changes were more transient: Subject B complained of fuzzy vision for four days after diving, but his acuity was unchanged; Subject S reported deterioration in one eye from 20/16 to 20/25 after the fifth dive, with complete resolution three days later. Subject U had a shift in acuity from 20/16 in both eyes to 20/20 in one and blurred vision in the other immediately after the five dives, with restoration four days after diving; Subject V changed from 20/20 in both eyes to 20/25 in both, with restoration four days after the last dive; and Subject Z's acuity changed in both eyes from 20/25 at baseline to 20/40 after the fifth day of diving, a change that had probably resolved the next day and certainly by three days after the fifth dive. Additionally, two subjects reported short-term improvements in distance vision, with or without loss of apparent accommodative power: Subject Q showed acuity changes from 20/20 at baseline to 20/16 after five dives and to 20/10 in one eye at three days after the fifth dive; and Subject N showed changes from 20/20 to 20/10 with deterioration in near vision. For all divers, acuity and near vision returned to baseline.

Effects on vision were much less pronounced when the six-hour dives occurred at 42-hour intervals, but they were not completely eliminated by the longer interval. Six days after the last dive, Subject X had a shift of -0.5 D in both eyes and an acuity change from 20/25, 20/30 at baseline to 20/30, 20/40, although we had measured no change on the fourth day after the dives. He was unaware of any change in vision, and his refraction was restored when we measured it two weeks later. Subject AC had a possible refraction change of -0.25 D and suffered from mildly irritated eyes the day after Dive 4. He also suffered moderately severe eye irritation before Dive 6. Subject A after Dive 3, Subject H after Dives 1 and 5, Subject M after Dive 4, and Subject AD after Dive 5 all complained of slightly blurry vision, but none had measurable changes in refraction.

EAR PROBLEMS

Three of the thirteen subjects (23%) who dove for two days in a row reported symptoms of gas absorption from the middle ear (Draeger ear) either between the dives (this report came from two subjects) or after the second dive. Additionally, one subject developed severe *otitis externa* four days after the second dive.

When the six-hour exposures each day were interrupted, the reported incidences of Draeger ear were subjectively, and sometimes statistically, greater than they were without the interruption: after the 2-hour surface interval dives, eight of twelve subjects (67%; Fisher's Exact $p = 0.047$, as compared to the uninterrupted dives) reported mild absorption syndrome, and one reported severe Draeger ear overnight after the second

dive and mild ear pain the next night. After the four-hour surface interval, fourteen of twenty-four subjects (58%) reported Draeger ear or ear congestion (Fisher's Exact $p = 0.042$ one-tailed, as compared to the uninterrupted dives), and two of them reported that the symptoms were moderate. After the six-hour surface interval dives, seven of twelve subjects (58%; not significantly different from the uninterrupted dives) reported Draeger ear.

During and after the five daily dives, eleven of sixteen subjects (69%; 95% CI: 41% to 89%) reported Draeger ear at some time, and for one it was severe. Six subjects also developed *otitis externa*, despite having used the aluminum acetic acid and solution after each dive.

The six-hour dives every other day provoked ear congestion or Draeger ear in twelve of the fifteen subjects (80%; 95% CI: 52% to 86%) after one or more dives. For one diver, the worst symptoms were moderate; for another one, moderately severe, and for a third, severe enough that he was forced to abort the dive series.

OTHER PROBLEMS

One of the subjects in the six-hour surface interval dives reported severe itching of arms and legs after diving. Five subjects in the series of five daily dives developed skin rashes, and for one of them the rash after the end of the dive series became debilitating, requiring medical attention for almost a week. One subject in the every-other-day series reported moderate itching between Dives 4 and 5 and mild itching between Dives 5 and 6.

After one day of diving for six hours, Subject I had moderate sleep disturbances, and after the second day he had severe sleep disturbances accompanied by a sense that he was threatened. Subject Q felt light-headed after the fifth dive of the daily series of five dives. Subject AK reported that he felt light-headed after each day of diving the split exposures with a two-hour surface interval. Subject AK also reported that he was irritable after each day of diving with the four-hour surface interval, and his irritability, because it was not relieved by eating, appeared to be unrelated to blood sugar levels. All symptoms abated gradually.

DISCUSSION

The incidences of mostly mild symptoms after one and two six-hour dives were greater than those after one and two 4-hour dives,^{3,6} while the incidences of flow-volume loop changes were low and not different either between one or two six- and four-hour dives or between single six- and eight-hour dives.⁹ There were no changes in diffusing capacity after one or two six-hour dives, while two divers had shown changes after two four-hour dives.⁶ During dives at $P_{O_2} = 1.35$ atm, oxygen insult accumulates sufficiently with time to generate more symptoms as duration increases but not sufficiently up to eight hours to reduce pulmonary function in many individuals.

We saw no accumulation of pulmonary injury from day to day even with five days of daily diving or two weeks of diving every other day, but symptoms or signs sometimes persisted until before the next dive. In some subjects, symptoms or signs present one day resolved before the next dive, and in some, they resolved during the next dive (Tables 4 and 5). This evidence of recovery is similar to that we reported after four-hour dives.⁶ The only evidence that some cumulative effects may have occurred is weak; the incidence of symptoms one or more days after the dive series was greater for five dives with 18 hours between them than for six dives with 42 hours between. An off-oxygen time of 18 hours appears sufficient to remove the direct products of the oxygen — but not, perhaps, to repair secondary injury.

The incidences of respiratory symptoms (Tables 4 and 5) were subjectively but not significantly lower when we increased the interval between dives from 18 to 42 hours. Fatigue and exercise intolerance, reported by 36% instead of 56% of the divers, also were subjectively but not significantly less common with the increased time between dives. Subjective results from the dives every other day in February 2004 differed from those conducted in August 2005, with subjects in the first series experiencing more symptoms and more fatigue than those in the second series. We confirmed that the breathing gas was 100% oxygen humidified both times, but we cannot rule out environmental confounders.

The incidences of respiratory signs and symptoms from the split daily exposures varied with the surface interval. With two three-hour dives, a two-hour surface interval, and sixteen hours overnight, the incidences of symptoms on either day — which did not differ from those after two daily six-hour dives — was marginally greater (Fisher's Exact $p = 0.06$) on the first day than it was after a single four-hour dive and was significantly greater after the second day of diving than it was after two four-hour dives (Fisher's Exact $p = 0.003$). The incidences of pulmonary function changes were not different among four- or six-hour dives and three-hour dives with a two-hour surface interval. Thus, two hours between dives does not appear to be sufficient for recovery from a three-hour dive of this kind: it makes "three hours on, two hours off, three hours on," equivalent to "six hours on."

With two three-hour dives, a four-hour surface interval, and fourteen hours overnight, significantly fewer divers reported symptoms than did those after diving for six hours with eighteen hours overnight. Indeed, the incidences of symptoms from the exposures split by a four-hour surface interval did not differ from corresponding incidences from two four-hour dives. The low incidence of pulmonary function changes was not different from either that for two six-hour dives or that for two four-hour dives. Thus, both the four-hour surface and the fourteen-hour overnight intervals seem to allow some recovery.

With two three-hour dives, a six-hour surface interval, and twelve hours overnight, the incidence of respiratory symptoms (not different from that for two six-hour dives) was no different on the first day from those incidences with a single four-hour dive (Fisher's

Exact $p = 0.45$), but this incidence was significantly greater on the second day than it was on the first day for a four-hour dive (Fisher's Exact $p = 0.04$). The six-hour surface interval seems to allow recovery during the day, but some effect appears to accumulate after the shorter overnight break. Paradoxically, flow-volume changes were more common on the first day with a six-hour surface interval than after either one six-hour dive (Fisher's Exact $p = 0.04$) or one four-hour dive (Fisher's Exact $p = 0.01$). However, if we consider that changes that had been present after three hours in one subject were gone after the second three-hour dive and consider only those changes present at the end of the dive day, three subjects showed flow-volume changes after the second dive of the day, a marginal increase in incidence from that after one six-hour dive (Fisher's Exact $p = 0.07$).

The split exposures, despite the few sample points and relatively small numbers of subjects, give some insight into the kinetics of symptom onset and recovery. Onset of symptoms seems somewhat sigmoidal as exposure time continues: the incidence of symptoms after one three-hour dive was 3/48 (6%; 95% binomial CI: 1%–17%) — not statistically different from 4/77 (5%; binomial CI: 1%–13%) for a single four-hour dive, but less than 19/52 (37%; binomial CI: 24%–51%) for a single six-hour dive. The incidence for a six-hour dive also was not statistically different from 10/23 (43%; binomial CI: 23%–66%) immediately after a single eight-hour dive.⁹ Healing seems to include a moderately fast component that effectively removes about two hours of exposure in about four hours: after a two-hour break, the second three-hour dive on the first day caused symptoms in significantly more people than the first (Fisher's Exact $p = 0.01$), but after a four-hour break, the second dive did not, and after a six-hour break, the second dive caused symptoms in marginally more subjects (Fisher's Exact $p = 0.09$). Healing seems to include a slow component as well: symptoms were more prevalent in the first dive of the second day than in the first dive of the first day only when the second dive on that first day produced significantly more symptoms than the first (i.e., for the two-hour surface interval and sixteen-hour overnight recovery; Fisher's Exact $p = 0.02$).

For the four-hour surface interval dives with fourteen hours overnight, the second-day incidences did not differ from those on the first day. A secondary cause of delayed symptoms may also exist, a cause for which symptoms are evident later only if healing earlier is incomplete: after a twelve-hour overnight interval, six hours between dives was no longer sufficient to make results for the second three-hour dive similar to those for the first (Fisher's Exact $p = 0.006$). Instead, the incidence of symptoms at day's end was like that for a single six-hour dive.

We saw fewer and smaller changes in flow-volume parameters than have been reported from head-out water immersion while breathing oxygen.¹⁰ The hydrostatic pressures acting on the lungs during these dives were like those for head-out immersion when the subjects were seated, but they were lower when the subjects reclined. Probably more important, though, acute changes in vital capacity from immersion involve translocation of blood and are very transient. All pulmonary function values that we report are the mean of three consistent efforts. If the first flow-volume loop maneuver resulted in lower

values than did subsequent attempts, the values from the first were discarded. Even if a first low reading was real, it was clearly mechanically reversible and thus not a sign of true toxicity. Furthermore, our measurements were made at least several minutes after the subjects had left the water. In the intervening time, they may have coughed, sighed, yawned, or performed Valsalva maneuvers to clear their ears. Normal readjustments of blood volume in the lungs probably had occurred in many cases before we measured vital capacity.

After two days with two three-hour dives each, reports of fatigue and exercise intolerance were not notably different from reports after two six-hour dives, except that the shortest SI resulted in no reports. These results are confounded by the work schedule. Because subjects began the workday at 0530 for the split exposure dives and were done no sooner than nine, eleven, or thirteen hours later for the two-, four-, or six-hour surface intervals, respectively, greater than normal fatigue was inevitable. Although we asked about "unreasonable fatigue," differentiating dive-related and schedule-related components is difficult. The absence of reports of fatigue from the shortest days with two three-hour dives and the trend to increased reports with increasing lengths of workday hint that work schedule holds a strong influence. That argument invites further conjecture that dive-related fatigue was reduced by interrupting the dives. However, in the real world, fatigue from any source reduces performance.

Some or all of the fatigue may result from immersion rather than from oxygen breathing. Water immersion causes increased excretion of water and sodium. In one twelve-hour water immersion study, losses on the order of 750 mL of water had accumulated after six hours of immersion even though the subjects had drunk 200 mL of water each hour during the study, and urinary sodium excretion at 5 hours of immersion was about three times the normal rate.¹¹ If losses of these magnitudes were only partly compensated each evening for several days in succession, the deficits could contribute to significant exercise intolerance and fatigue. Thirst is driven more by relative excesses of salt than by volume depletion. Furthermore, for subjects with moderate to severe middle ear absorption syndrome, discomfort upon swallowing also could be a disincentive to full rehydration.

Repeated six-hour dives at an oxygen partial pressure of 1.35 atm can significantly change visual acuity and refraction. The exposure from two days of diving appears to be safe for the eyes, but five days with an 18-hour interval provokes changes at a frequency that is worrisome. With the 42-hour off-oxygen time, effects on vision were considerably less severe than those with the 18-hour interval, but effects were still not absent. Individual susceptibility may be important; the subject with a myopic shift in the series of dives every other day had undergone a similar change in acuity after the series of five daily dives. Until we know more about thresholds for hypoxic change, monitoring refraction before and after repeated high P_{O_2} dives appears to be important.

Middle ear gas absorption was a significant problem in many of these dives. Ear pain forced one diver to withdraw from the six-day, every-other-day dive series, and it was sufficient to have kept another diver from the water if he had been planning on three

days rather than two in a short SI dive. It is counterintuitive that interrupting a dive with a short SI increases the incidence of Draeger ear. Perhaps subjects slept more deeply because of the work schedules for those dives and, waking only when their ears had become painful, they failed to wake and clear their ears when their ears felt "full."

The skin problems were most likely related to repeated, prolonged water immersion rather than to oxygen exposures. The water quality in the test pool was maintained to standards for swimming pools, but 30 to 36 hours of soaking in a warm swimming pool is probably sufficient to break down the natural barriers of the skin.

The symptoms that might have been central nervous system effects of oxygen must not be disregarded. Although these symptoms were minor and affected only three subjects, in two cases they could have negatively affected judgment. Subtle changes, even if they affect only susceptible individuals, may have important consequences for operational activity.

CONCLUSIONS

Diving with $P_{O_2} = 1.35$ atm for six hours in a 24-hour period is not unworkable but still must be approached with some caution. Pulmonary oxygen toxicity itself, though measurable, seems to be more a nuisance than a real problem for this exposure. Single six-hour dives provoke respiratory symptoms, mostly mild, about twice as often as do the currently accepted four-hour dives, but pulmonary function changes are few and of similar frequency and magnitude to those from four-hour dives. The incidences and severity of respiratory symptoms or changes in pulmonary function do not increase as the number of dives increases either for daily diving or for diving every other day, and changes that occur after one dive may resolve before or during the next. However, multiple six-hour dives are very fatiguing, and they provoke greater exercise intolerance than do multiple four-hour dives. They also may precipitate other forms of oxygen injury: possibly subtle central nervous system disturbances and definitely changes in vision. Hyperoxic myopia was found after the series of five daily dives and after the series of six dives every other day. It showed delayed onset in several cases and resolved spontaneously over a period of at least one week.

Splitting the daily exposure of six hours into two three-hour dives reduces respiratory symptoms on a dive day if the SI is four hours or more, but an overnight interval greater than twelve hours is needed if reductions of symptoms are to continue into the second day. We do not know the effects of a short SI on hyperoxic myopia because we dove the protocol for only two days, but irritability and light-headedness were associated with two three-hour dives in one day.

Middle ear absorption syndrome is a mechanical effect of oxygen chemistry rather than a direct toxic effect. It remains a distinct problem for six-hour oxygen exposures — and particularly for repeated ones.

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